Ocular Muscle Physiology

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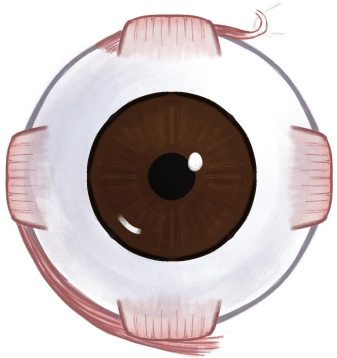


Neuromuscular Junction

Demyelinating disorders

Action potential from brain

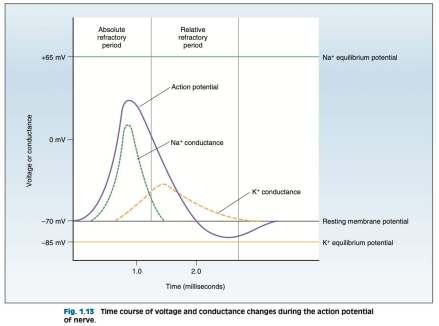


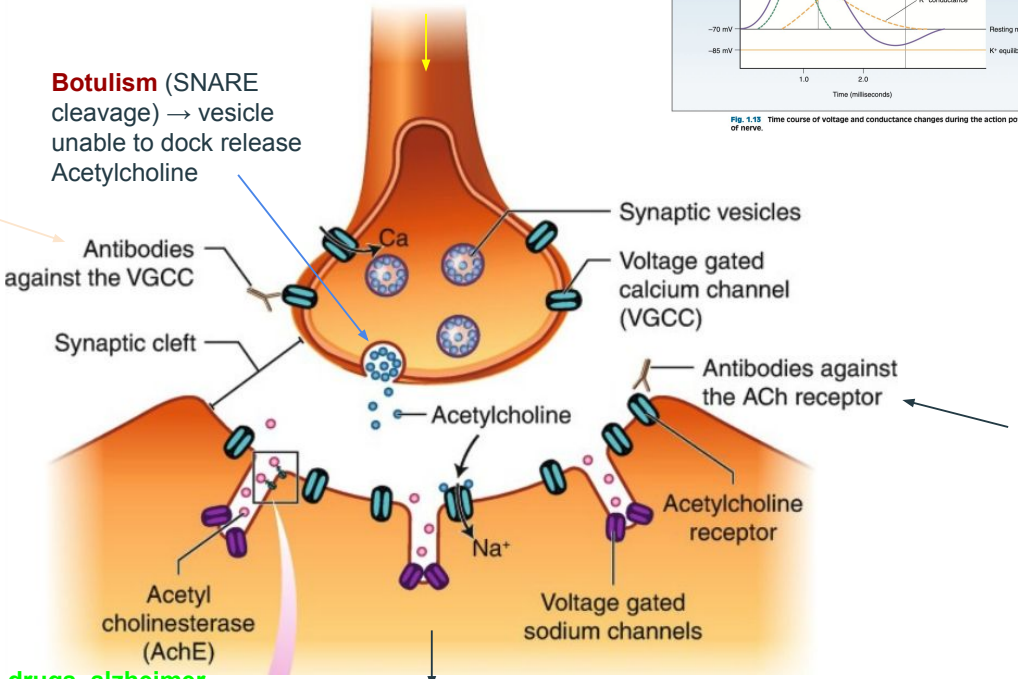
Fig. 1.13 Time course of voltage and conductance changes during the action potential of nerve.

Electrolytes involved Na, K Disturbances can cause pathology

Image: Costanzo

Botulism (SNARE cleavage) → vesicle unable to dock release Acetylcholine

Lambert Eaton Syndrome → Presynaptic receptor blockade → Calcium unable to enter, no ACh release



Myasthenia gravis → ACh Postsynaptic Receptor blockade → no calcium release

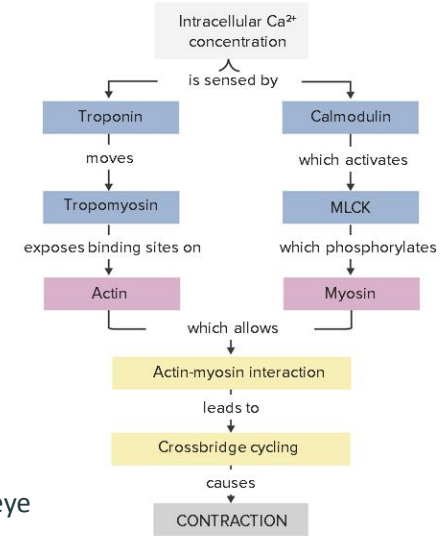
Organophosphate, MG drugs, alzheimer drugs

Calcium release

@ NMJ → calcium released → muscle fiber → 2 major pathways

Muscle Fiber Types in Eyes & Overview

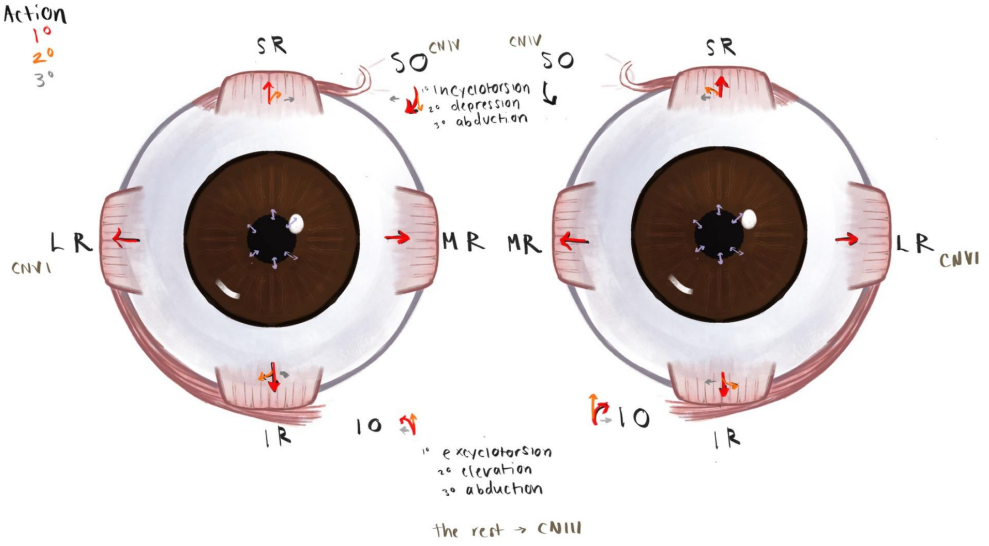
Striated muscle



Smooth muscle

Mainly fast twitch, glycolytic subtype in eye

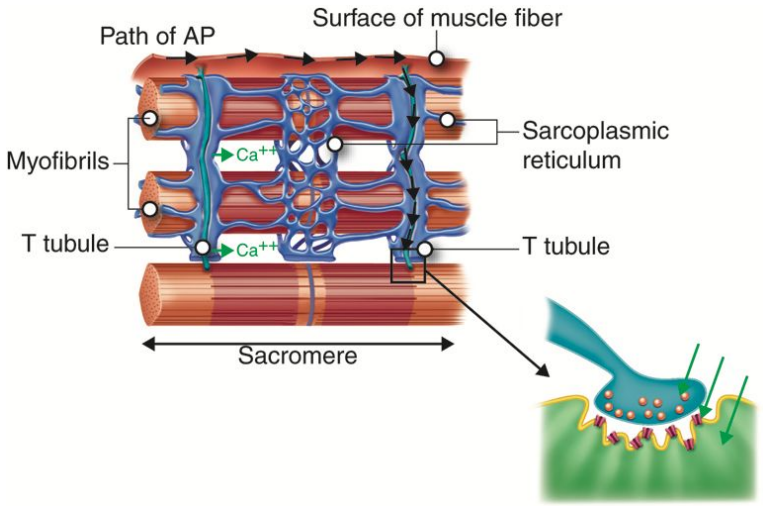
Left Diagram: Lecturio https://www.lecturio.com/concepts/smooth-muscle-contraction/



Voluntary Skeletal/Striated Muscle - Structure

Aka muscle cell (multinucleate due to merging)

Closer look at the **sarcomere**, contractile unit



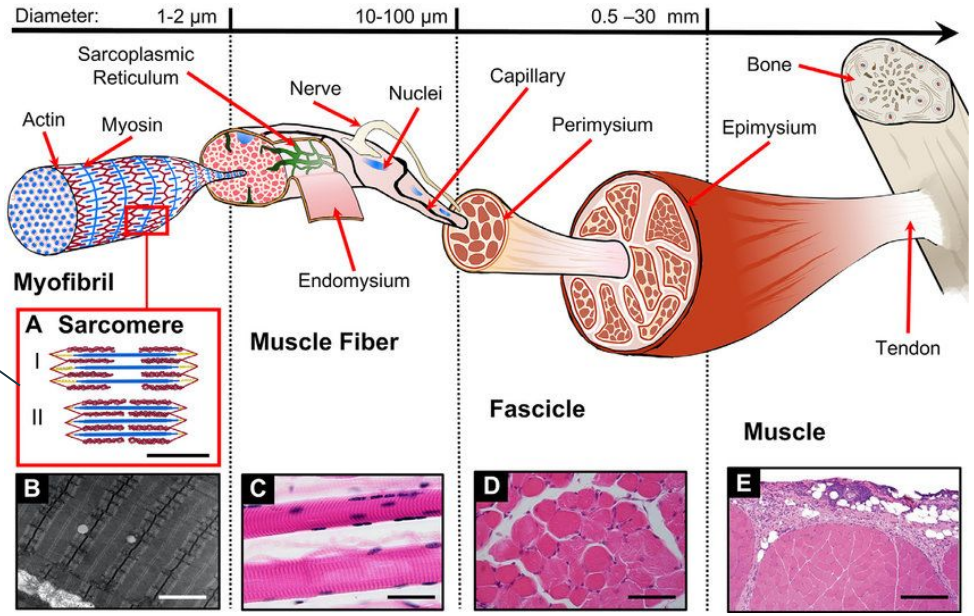


Image: Hierarchical structure of skeletal muscle. A) Sarcomere morphology and sliding mechanism (Scalebar 0.5 nm): Actin (red), Myosin (blue) and Titin (yellow) filaments are shown in the relaxed state (I) and during the contraction (II). The jagged sides represent the Z-lines. The central space without actin filaments is the H zone. B) Transmission Electron Microscopy (TEM) image of myofibrils (scalebar = 1 nm. Reproduced under CC0 1.0 Universal Public Domain Dedication. Author: Louisa Howard). C) Phase Contrast Microscope (PCM) image of skeletal muscle fibers. Dark violet elliptical elements are the myocytes nuclei (scalebar = 50 µm. Reproduced under CC0 1.0 Universal Public Domain Dedication. Author: Berkshire Community College). D) Histological image of a fascicle cross-section. Larger white bands are the perimysium membranes. Circular structures are the muscle fibers, while the darker violet dots are the myocytes nuclei (scalebar = 100 µm. Reproduced under Attribution-ShareAlike 3.0 Unported. Author: Ganimedes). E) Histological image of a portion of muscle cross-section. In the upper part, the epimysium membrane is visible (scalebar = 0.5 mm. adapted from [170] , reproduced under permission. Copyright 2008, Elsevier B.V.).

Image: by Cenveo Creative Commons 3

Striated Muscle Contraction

Simultaneous cross bridging contracts sarcomere

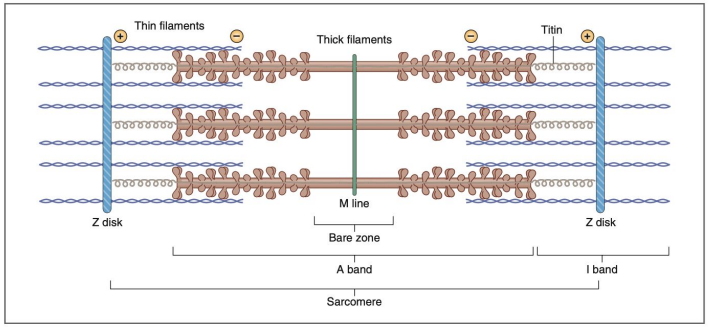
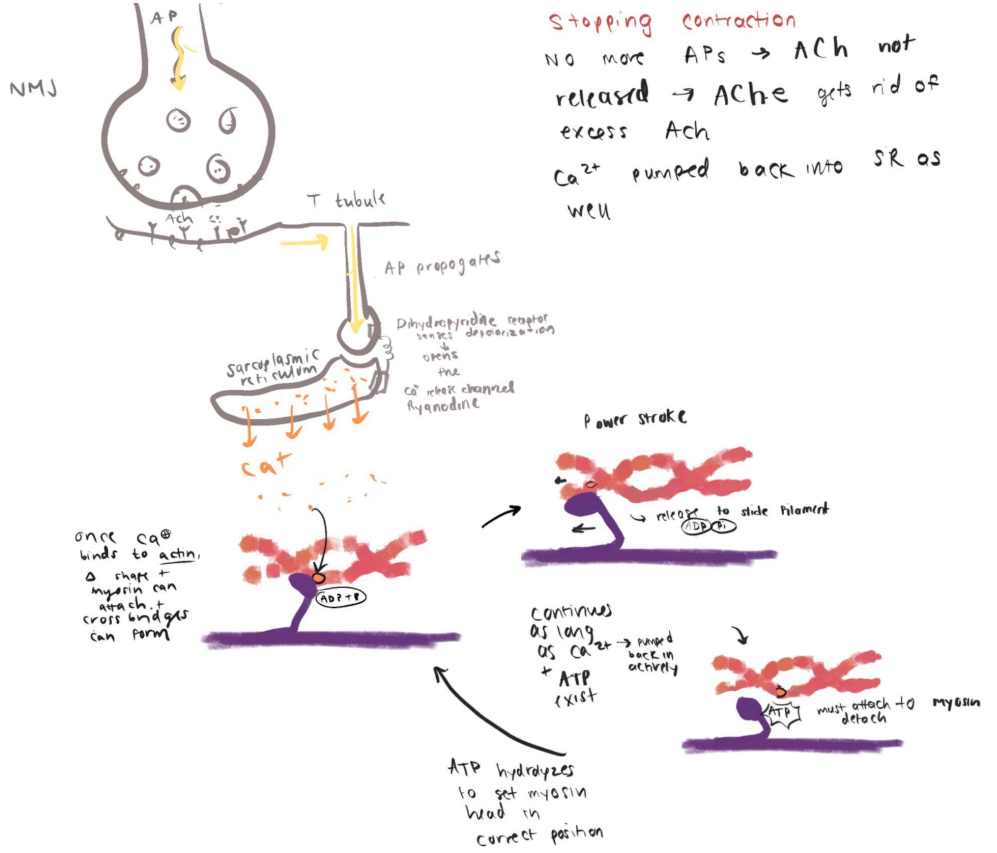


Fig. 1.22 **Arrangement of thick and thin filaments of skeletal muscle in sarcomeres.**

Image: L. Costanzo Physiology

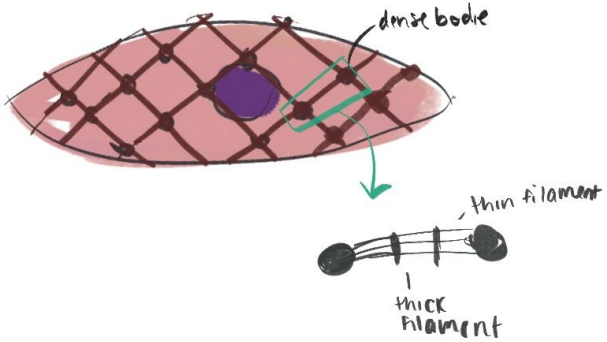


[Alila medical has a great animation for visualizing]

Smooth muscle structure

Smooth Muscle Cell

Uni-nucleate



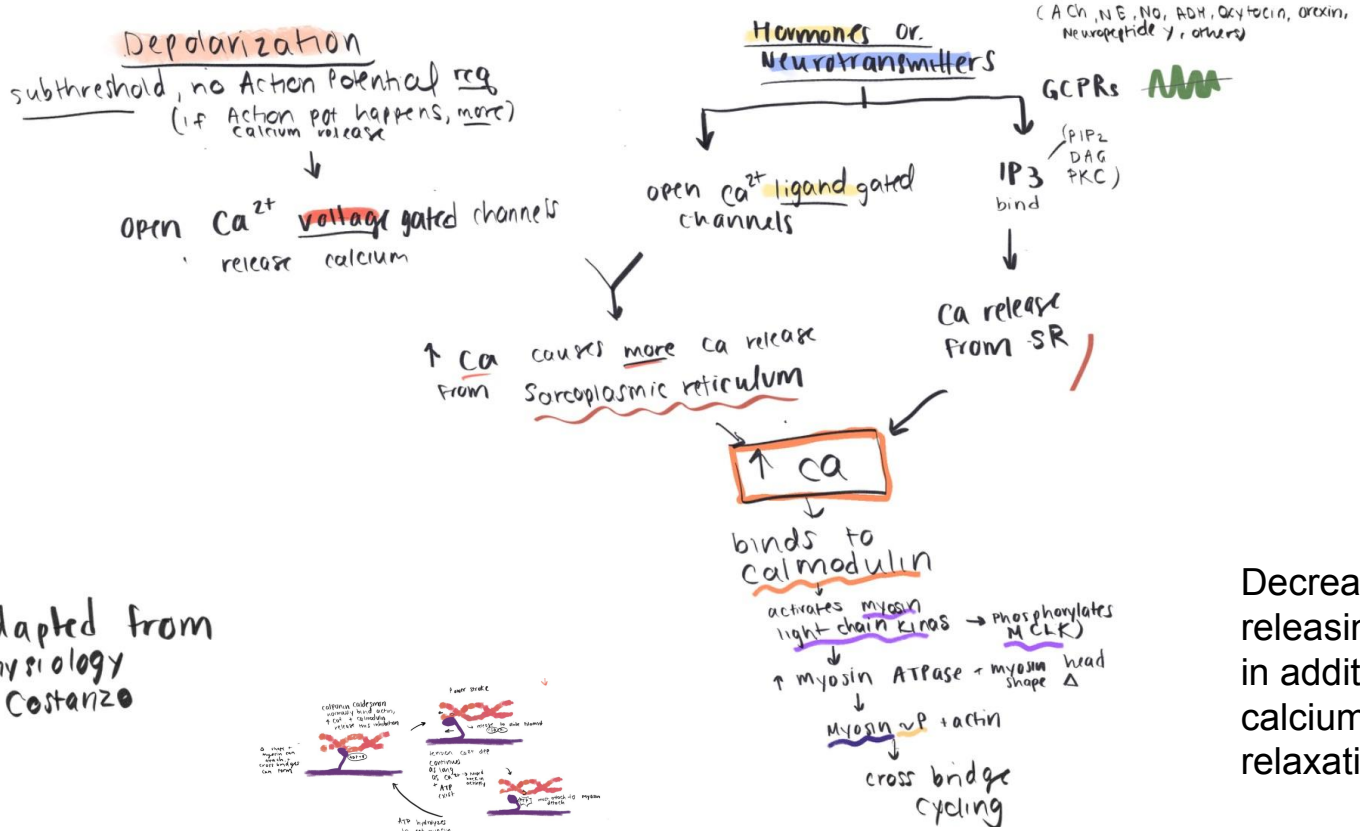
- multi unit in eye →

Iris Smooth Muscle configuration

constrictor circular

dilator radial

Smooth Muscle Contraction



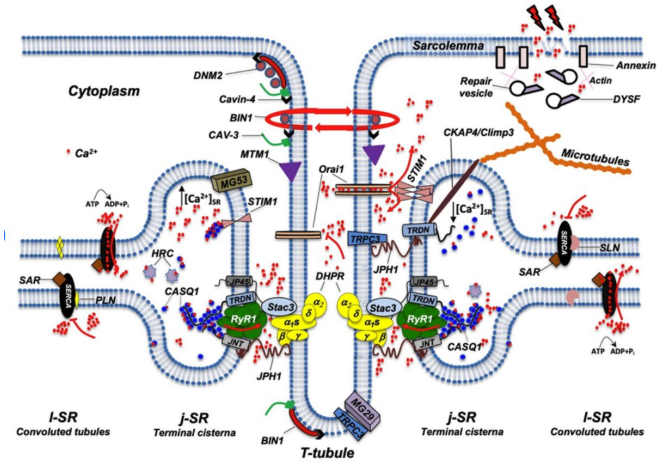
Adapted from physiology L. Costanzo

Decrease in any Ca2+ releasing mechanisms above in addition to active pumping calcium back into SR → relaxation

Pathophys Factors Affecting Ocular Muscles Recap

- **Vascular** → aneurysm or ischemia can affect nerves (rarer in peds, but possible vascular etiologies in kids sickle cell, very poorly controlled T1 DM, dissection (falling onto toothbrush, trauma)
  - palsies/pupil abnormalities (PPP mnemonic peripheral parasympathetic pupil affected)
- **Iatrogenic/Infectious/Inflammatory**
  - Orbital cellulitis, Trichinellosis, etc
- **Nutritional** → electrolyte disturbances, synthesize hormones, neurotransmitters, proteins
  - picky eaters, sports exertion and/or heat exhaustion/stroke
- **Neoplastic** → neuroblastoma (opsoclonus-myoclonus, horner's syndrome), retinoblastoma,
- **Congenital/Developmental disorders** → myotonic dystrophy commonly causing ptosis for example, congenital ptosis
- **Mitochondria** → Leber hereditary optic neuropathy is also mitochondrial disease
- **Toxic substances** → exposures rare but possible organophosphates, cocaine, PCP, opiates, bio weapons,
- **Trauma** → common in peds
- **Autoimmune** → MG, TED, sometimes in other systemic autoimmune conditions
- **Nerves** → demyelinating disease - NMO, MS, Guillain Barre, Botulism, compressive factors

Quite a complex process



Schematic representation of the main proteins accommodated in TT, j-SR, and l-SR. Protein localization and reciprocal interactions are schematized as detailed in the text. Red arrows indicate Ca^{2+} fluxes (red dots) through RyR1, Orai1, and SERCA pumps. RyR1 opens following interaction with DHPR; Orai1 opens following interaction with STIM1 aggregates, which in turn are induced by a reduction in Ca^{2+} levels in the SR; SERCA pumps actively transport Ca^{2+} from the cytosol to l-SR; PLN or SLN act as SERCA inhibitors. DNM2, Cavin-4, BIN1, CAV-3, and MTM1 are involved in the maintenance of TT architecture and stability. They also participate in TT formation (not shown) and, together with DYSF, contribute to vesicle trafficking during the repair of the damaged plasma membrane (see text for additional details). For simplicity, not all proteins and/or protein complexes depicted, including cytoskeleton components, are positioned on both sides of the triad, as it occurs physiologically. The following is a list of acronyms depicted in Figure 3: BIN1 (Bridging integrator-1/Amphiphysin 2); CASQ1 (Calsequestrin 1); CAV-3 (Caveolin-3); CKAP4 (Cytoskeleton-associated protein 4/Climp63); DHPR (dihydropyridine receptor); DNM2 (Dynamin 2); DYSF (Dysferlin); HRC (Histidine-Rich Calcium binding protein); JNT (Junctin); JP45 (J-SR protein 1); JPH1 (Junctophilin 1); j-SR (junctional sarcoplasmic reticulum); l-SR (longitudinal sarcoplasmic reticulum); MG29 (Mitsugumin-29); MG53 (Mitsugumin-53); MTM1 (Myotubularin); PLN (Phospholamban); RyR1 (Type 1 Ryanodine Receptor); SAR (Sarcalumenin); SERCA (Sarco/Endoplasmic Reticulum Calcium ATPase); SLN (Sarcolipin); STIM1 (Stromal Interaction Molecule 1); TRDN (Triadin); TRPC3 (Transient Receptor Potential Cation Channel 3); T-tubule (transverse tubule). Adapted from [23].

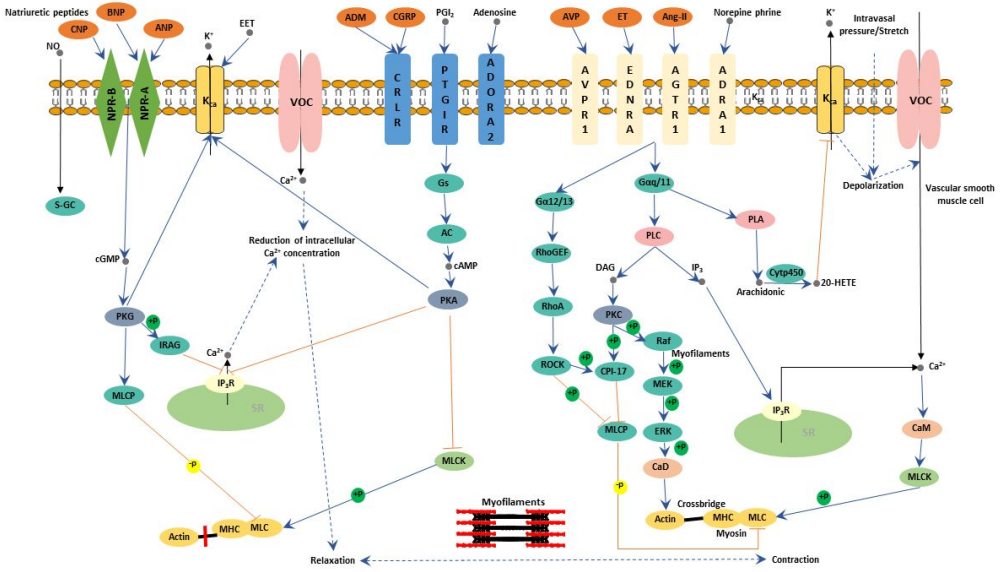


Image: Cusabio

References

Physiology, 6e. Lippincott Williams & Wilkins, a Wolters Kluwer bu; 2015.

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